

## REMARKS

1. Rejection of Claims 27-33 and 37-38 under 35 U.S.C. 101 and under 35 U.S.C. 112, first paragraph.

Claims 27-33 and 37-38 were rejected under 35 U.S.C. 101 and under 35 U.S.C. 112, first paragraph as lacking patentable utility and for failing to comply with the written description requirement, as set forth in the Office Action. Due to the overlapping issues presented by the examiner under each of these code sections, Applicants have chosen to combine this response into a single argument.

Initially, Applicants note that independent Claim 27 has been canceled and independent Claim 37 has been amended such that the pending claim scope recites nucleic acid molecules that encode a protein having amino acid SEQ ID NO:1873 and proteins that are at least 95% identical to SEQ ID NO:1873, where such proteins have chloride channel activity.

Applicants respectfully traverse the Examiner's arguments and argue that the application sets forth patentable utility as set forth in the guidance provided by the USPTO's Revised Interim Utility Guidelines Training Materials, and in particular, Example 10. According to this Example, when a claimed sequence shows significant homology to a known family of proteins, and the next most homologous protein outside the family has a significantly lower homology and an unrelated function, then there is "no reason to doubt" the claimed protein has the function of the proteins in the family. Applicants have attached protein alignments showing that the highest 40 hits representing characterized proteins are chloride channel proteins. Accordingly, Applicant contends that given the stated identities and availability of data regarding highly related families of proteins, one of skill in the art would place the protein encoded by the claimed nucleic acid molecule in the chloride channel family. Regarding the nucleic acid sequence alignments

provided by the Examiner, Applicants respectfully note that the alignments do not provide any “reason to doubt” that the claimed nucleic acid molecules encode chloride channels because those alignments are to reverse strands relative to the nucleic acid molecules of the present invention and therefore probably do not even encode proteins, much less a protein that would cast doubt upon the identity of proteins of the present invention. One of skill in the art would recognize that protein sequence alignments, such as those provided by the applicants, are much more persuasive indicators of a protein’s identity.

Applicants further argue that the present claims and specification satisfy the requirements of 35 U.S.C. 112, 1<sup>st</sup> paragraph for written description. Applicants have attempted to follow the model as set forth in Training Example No. 14 of the Synopsis of Application of Written Description Guidelines, which was prepared by the USPTO to train Examiners how to apply the requirements set out in Federal Register, Vol. 66, No. 4, pages 1099-1111.

The Examiner cited *Regents of the University of California v. Eli Lilly and Company*, 119 F3d 1559 (“*Lilly*”) which generally stands for the proposition that a description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Although the Examiner’s arguments were specifically directed to former Claim 27, Applicants assume the Examiner also intended to direct the arguments to Claim 29, which is the current independent claim. Applicants respectfully disagree that the present claims lack adequate written description in view of *Lilly*. The specification describes 2 nucleic acid molecules that encode protein sequence SEQ ID NO:1873 and variants thereof where such variants are highly structurally related to the claimed nucleic acid molecules in that they must

possess at least 95% sequence identity and must be sufficiently similar structurally to possess the same activity. Applicants respectfully argue that the present specification satisfies the requirements of 35 U.S.C. 112, first paragraph and direct the Examiner to the guidance provided by Example No. 14 of the Synopsis of Application of Written Description Guidelines, which was prepared by the USPTO to train Examiners how to apply the requirements set out in Federal Register, Vol. 66, No. 4, pages 1099-1111.

Training Example 14 describes a hypothetical specification which discloses a single protein species, SEQ ID NO:3, which catalyzes the reaction of A to B. The specification contemplates, but does not exemplify, variants having the same activity. The specification further indicates that procedures for making variants are routine and provides an assay for testing such variants for activity. Based upon the foregoing, the applicant in Example 14 claims a protein having SEQ ID NO:3 and variants that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A to B.

Applicants note that the USPTO analysis correctly concludes that description of the necessary common attributes of the genus is what is required to satisfy 35 U.S.C. 112, first paragraph, and not physical possession of some arbitrary number of species exhibiting that activity. Accordingly, Applicants respectfully assert, and argue that the USPTO analysis concurs, that a single disclosed species can adequately define a genus of structurally similar molecules having the same functional property, and is thus consistent with the requirements as set forth in *Lilly* 119 F3d at 1569, 43 USPQ2d at 1406, which calls for "recitation of a representative number of polypeptide sequences \*\*\* **or of a recitation of structural features common to the genus**" (emphasis added).

Applicant's similarly argue that *Fiers v. Revel* 25 USPQ2d 1601 ("*Fiers*") does not support the present rejection. The issue in *Fiers* was a determination of priority in an interference proceeding among three competing applicants (Fiers, Revel and Sugano) each seeking patent protection for human beta-interferon nucleic acids and proteins. In deciding which applicant had the earliest priority claim, the court reviewed the parent cases for sufficiency of written description. The court decided that neither Fiers nor Revel had satisfied the written description requirement of the first paragraph of 35 U.S.C. 112 because, in each case, the applicants had failed to disclose even a single nucleic acid or amino acid sequence, but rather had based their claims to nucleic acid sequences upon disclosure of methods to isolate such sequences. It is the court's discussion of the inadequacies of the Fiers and Revel applications that the Examiner cites in the instant application. In contrast, the court found that Sugano's priority case "satisfies the written description requirement since it sets forth the complete and correct nucleotide sequence of a DNA coding for B-IF" *Fiers* at 1607. Accordingly, Applicants respectfully argue that the citation of a small portion of the court's discussion relating to the two cases which contained no sequence information to attack the breadth of the instant claims is a misapplication of *Fiers*. Similar to the Sugano application, the instant application contains a disclosure of a complete and correct sequence. Accordingly, Applicants argue that the court's discussion of the Sugano application, and therefore the ultimate ruling of *Fiers*, supports the Applicants' argument that the instant claims are adequately supported. In fact, once interference proceedings were concluded and Sugano was allowed to prosecute his case, the written description contained therein was found sufficient to support claims covering nucleic acid molecules other than the sequences specifically disclosed (See claim 1 of U.S. Patent No

5,326,859, which reads "A DNA which consists essentially of a DNA which codes for human fibroblast  $B_1$  interferon polypeptide").

In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of Claims 27-33 and 37-38 under 35 U.S.C. 101 and under 35 U.S.C. 112, first paragraph.

In the event the Examiner has any questions regarding this application, the Examiner is invited to contact the Applicants' undersigned representative.

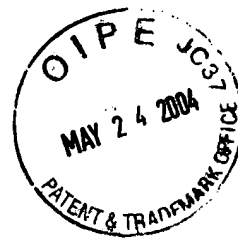
Respectfully submitted,

Dated: May 21, 2004



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Facsimile: (970) 491-9976



## Related Structures

Sequences producing significant alignments:

	Score (bits)	E Value
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	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=45360517[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=45360517[pgi]</a>			
<input type="checkbox"/>	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=45360517[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=45360517[pgi]</a>			
	gi 47086677 ref NP_997847.1	Unknown (protein for MGC:77044...	<u>89</u>	9e-17
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=47086677[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=47086677[pgi]</a>			
<input type="checkbox"/>	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=47086677[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=47086677[pgi]</a>			
	gi 31455211 gb AAH05367.1	CLIC2 protein [Homo sapiens]	<u>88</u>	2e-16
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=31455211[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=31455211[pgi]</a>			
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=31455211[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=31455211[pgi]</a>			
	gi 47208023 emb CAF90034.1	unnamed protein product [Tetrao...	<u>87</u>	5e-16
<input type="checkbox"/>	gi 32396202 gb AAP41072.1	chloride intracellular channel p...	<u>84</u>	3e-15
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=32396202[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=32396202[pgi]</a>			
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=32396202[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=32396202[pgi]</a>			
<input type="checkbox"/>	gi 47218613 emb CAG04942.1	unnamed protein product [Tetrao...	<u>83</u>	4e-15
	gi 16518424 gb AAL24813.1	chloride intracellular channel 6...	<u>79</u>	7e-14
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16518424[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16518424[pgi]</a>			
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16518424[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16518424[pgi]</a>			
	gi 39582729 emb CAE65935.1	Hypothetical protein CBG11108 [...	<u>79</u>	8e-14



☐ [gi|21751399|dbj|BAC03959.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=21751399[pgi]) unnamed protein product [Homo s... 78 1e-13  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=21751399\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=21751399[pgi])

☐ [gi|12857232|dbj|BAB30940.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=12857232[pgi]) unnamed protein product [Mus mu... 74 2e-12  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=12857232\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=12857232[pgi])

☐ [gi|38077746|ref|XP\\_357350.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=38077746[pgi]) similar to intracellular chlor... 74 3e-12  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=38077746\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=38077746[pgi])

☒ [gi|39654881|pdb|1RK4|A](http://www.ncbi.nlm.nih.gov/Structure/cblast/cblast.cgi?blast_RID=1084988551-21298-150072222312.BLASTQ3&blast_rep_gi=39654881&hit=39654881&blast_CD_RID=1084988551-21298-208513172011.BLASTQ3&blast_view=onegroup&hsp=0&taxname=none&client=blast) Chain A, Crystal Structure Of A Solu... 71 2e-11  
[http://www.ncbi.nlm.nih.gov/Structure/cblast/cblast.cgi?blast\\_RID=1084988551-21298-150072222312.BLASTQ3&blast\\_rep\\_gi=39654881&hit=39654881&blast\\_CD\\_RID=1084988551-21298-208513172011.BLASTQ3&blast\\_view=onegroup&hsp=0&taxname=none&client=blast](http://www.ncbi.nlm.nih.gov/Structure/cblast/cblast.cgi?blast_RID=1084988551-21298-150072222312.BLASTQ3&blast_rep_gi=39654881&hit=39654881&blast_CD_RID=1084988551-21298-208513172011.BLASTQ3&blast_view=onegroup&hsp=0&taxname=none&client=blast)

☐ [gi|22761044|dbj|BAC11432.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=22761044[pgi]) unnamed protein product [Homo s... 70 5e-11  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=22761044\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=22761044[pgi])

☐ [gi|15617203|ref|NP\\_254279.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=15617203[pgi]) chloride intracellular channel... 70 5e-11  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=15617203\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=15617203[pgi])

☐ [gi|6685316|sp|Q9XSA7|CLI4\\_BOVIN](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=6685316[pgi]) Chloride intracellular chan... 70 6e-11  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=6685316\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=6685316[pgi])

☒ [gi|17943341|pdb|1K00|A](http://www.ncbi.nlm.nih.gov/Structure/cblast/cblast.cgi?blast_RID=1084988551-21298-150072222312.BLASTQ3&blast_rep_gi=17943341&hit=17943341&blast_CD_RID=1084988551-21298-208513172011.BLASTQ3&blast_view=onegroup&hsp=0&taxname=none&client=blast) Chain A, Crystal Structure Of A Solu... 69 7e-11  
[http://www.ncbi.nlm.nih.gov/Structure/cblast/cblast.cgi?blast\\_RID=1084988551-21298-150072222312.BLASTQ3&blast\\_rep\\_gi=17943341&hit=17943341&blast\\_CD\\_RID=1084988551-21298-208513172011.BLASTQ3&blast\\_view=onegroup&hsp=0&taxname=none&client=blast](http://www.ncbi.nlm.nih.gov/Structure/cblast/cblast.cgi?blast_RID=1084988551-21298-150072222312.BLASTQ3&blast_rep_gi=17943341&hit=17943341&blast_CD_RID=1084988551-21298-208513172011.BLASTQ3&blast_view=onegroup&hsp=0&taxname=none&client=blast)

☐ [gi|2073569|gb|AAC25675.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=2073569[pgi]) nuclear chloride ion channel prot... 69 9e-11  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=2073569\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=2073569[pgi])

☐ [http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=2073569\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=14251209[pgi])  
[gi|14251209|ref|NP\\_001279.2|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=14251209[pgi]) chloride intracellular channel... 69 9e-11  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=14251209\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=14251209[pgi])

☐ [gi|38511628|gb|AAH60967.1|](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=38511628[pgi]) Clic3 protein [Mus musculus] 69 1e-10  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=38511628\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=38511628[pgi])

<input type="checkbox"/>	<a href="#">gi 27229085 ref NP_081361.1 </a> chloride intracellular channel...	<a href="#">69</a>	1e-10
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27229085[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27229085[pgi]</a>		
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27229085[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27229085[pgi]</a>		
<input type="checkbox"/>	<a href="#">gi 46237607 emb CAE83985.1 </a> chloride intracellular channel ...	<a href="#">68</a>	1e-10
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=46237607[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=46237607[pgi]</a>		
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=46237607[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=46237607[pgi]</a>		
<input type="checkbox"/>	<a href="#">gi 7499974 pir T21429</a> hypothetical protein F26H11.5 - Caen...	<a href="#">68</a>	2e-10
	<a href="#">gi 17533495 ref NP_497000.1 </a> chloride intracellular channel...	<a href="#">68</a>	2e-10
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=17533495[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=17533495[pgi]</a>		
<input type="checkbox"/>	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=17533495[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=17533495[pgi]</a>		
	<a href="#">gi 34853013 ref XP_238312.2 </a> similar to chloride intracellu...	<a href="#">67</a>	3e-10
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34853013[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34853013[pgi]</a>		
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34853013[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34853013[pgi]</a>		
	<a href="#">gi 46394424 gb AAS91556.1 </a> chloride intracellular channel p...	<a href="#">65</a>	1e-09
<input type="checkbox"/>	<a href="#">gi 24211549 sp Q95MF9 CLI1_RABIT</a> Chloride intracellular cha...	<a href="#">65</a>	1e-09
	<a href="#">gi 40288290 ref NP_004660.2 </a> chloride intracellular channel...	<a href="#">65</a>	1e-09
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=40288290[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=40288290[pgi]</a>		
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=40288290[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=40288290[pgi]</a>		
	<a href="#">gi 22653413 gb AAN04048.1 </a> dehydroascorbate reductase [Bras...	<a href="#">64</a>	4e-09
	<a href="#">gi 46093477 dbj BAD14935.1 </a> dehydroascorbate reductase [Bra...	<a href="#">63</a>	7e-09
	<a href="#">gi 33338084 gb AAQ13664.1 </a> MSTP130 [Homo sapiens]	<a href="#">61</a>	3e-08
	<a href="#">gi 22653415 gb AAN04049.1 </a> dehydroascorbate reductase [Bras...	<a href="#">61</a>	3e-08
	<a href="#">gi 18418055 ref NP_568336.1 </a> dehydroascorbate reductase, pu...	<a href="#">60</a>	4e-08
	<a href="#">gi 10952514 gb AAG24946.1 </a> dehydroascorbate reductase [Arab...	<a href="#">60</a>	5e-08
<input type="checkbox"/>	<a href="#">gi 17473687 gb AAL38300.1 </a> unknown protein [Arabidopsis tha...	<a href="#">60</a>	5e-08
	<a href="#">gi 7022992 dbj BAA91794.1 </a> unnamed protein product [Homo sa...	<a href="#">59</a>	8e-08
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7022992[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7022992[pgi]</a>		
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7022992[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7022992[pgi]</a>		
	<a href="#">gi 28192425 gb AAL71856.1 </a> dehydroascorbate reductase [Oryz...	<a href="#">59</a>	1e-07
	<a href="#">gi 6939839 dbj BAA90672.1 </a> GSH-dependent dehydroascorbate r...	<a href="#">58</a>	2e-07
	<a href="#">gi 10952512 gb AAG24945.1 </a> dehydroascorbate reductase [Spin...	<a href="#">56</a>	8e-07
	<a href="#">gi 28192421 gb AAL71854.1 </a> dehydroascorbate reductase [Trit...	<a href="#">55</a>	2e-06
	<a href="#">gi 15223576 ref NP_173387.1 </a> dehydroascorbate reductase, pu...	<a href="#">54</a>	3e-06
	<a href="#">gi 28192427 gb AAL71857.1 </a> dehydroascorbate reductase [Nico...	<a href="#">53</a>	6e-06
<input type="checkbox"/>	<a href="#">gi 25402899 pir D86328</a> protein F18014.33 [imported] - Arab...	<a href="#">52</a>	1e-05
	<a href="#">gi 895845 emb CAA61020.1 </a> p64 CLCP [Homo sapiens]	<a href="#">52</a>	1e-05
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=895845[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=895845[pgi]</a>		
<input type="checkbox"/>	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=895845[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=895845[pgi]</a>		
	<a href="#">gi 4323622 gb AAD16450.1 </a> intracellular chloride channel CL...	<a href="#">51</a>	2e-05
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=4323622[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=4323622[pgi]</a>		
	<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=4323622[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=4323622[pgi]</a>		
	<a href="#">gi 11271417 pir T51503</a> valine-tRNA ligase-like protein - A...	<a href="#">50</a>	3e-05
	<a href="#">gi 26343937 dbj BAC35625.1 </a> unnamed protein product [Mus mu...	<a href="#">50</a>	4e-05
	<a href="#">gi 15239354 ref NP_198476.1 </a> dehydroascorbate reductase, pu...	<a href="#">49</a>	9e-05

gi 28394755 gb AAO38670.1	chloride intracellular channel 2...	48	2e-04
gi 33285914 gb AAQ01573.1	putative dehydroascorbate reduct...	48	2e-04
gi 21593056 gb AAM65005.1	GSH-dependent dehydroascorbate r...	45	0.001

□

gi 15222163 ref NP_177662.1	dehydroascorbate reductase, pu...	45	0.001
gi 34852289 ref XP_345084.1	similar to CLCP [Rattus norveg...	45	0.001
<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34852289[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34852289[pgi]</a>			
<a href="http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34852289[pgi]">http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=34852289[pgi]</a>			
gi 15223575 ref NP_173386.1	dehydroascorbate reductase, pu...	45	0.001
gi 3121851 sp Q29238 CLI1_PIG	Chloride intracellular channe...	41	0.025
gi 32395732 gb AAO63160.1	thiol transferase Tc52 [Trypanos...	37	0.47
gi 32395934 gb AAO63165.1	thiol transferase Tc52 [Trypanos...	36	0.63
gi 537611 gb AAA21419.1	TcAc2 >gi 1090533 prf  2019263A gl...	36	0.65

31200367  
 >gi|31200367|ref|XP\_309131.1| ENSANGP00000024624 [Anopheles gambiae]  
 gi|30178540|gb|EAA45365.1| ENSANGP00000024624 [Anopheles gambiae str. PEST]

Length = 299

Score = 441 bits (1135), Expect = e-123  
 Identities = 218/262 (83%), Positives = 232/262 (88%), Gaps = 8/262 (3%)

Query: 1 MSDEMQENG-TINGEVPEIELIIKASTIDGRRKGACLFCEYFMDLYLLAELKTISLKVT 59  
 MSDE Q+NG + NG VPEIELIIKASTIDGRRKGACLFCEYFMDLYLLAELKTISLKVT  
 Sbjct: 5 MSDEGQDNGASRNGSVPEIELIIKASTIDGRRKGACLFCEYFMDLYLLAELKTISLKVT 64

Query: 60 TVDMQKPPPDFRTNFEATPPPILIDNGLAVLENDKIERHIMKSVPGGHNLFVQDKEVATL 119  
 TV MQKPPPDFRTNFEAT PPILIDNGLA+LEN+KIERHIMKSVPGG+NLVQDKEVATL  
 Sbjct: 65 TVCMQKPPPDFRTNFEATHPPILIDNGLAILENEKIERHIMKSVPGGYNLFVQDKEVATL 124

Query: 120 IENLYSXXXXXXXXXXXXXXXXXSNLLSHLRKINDHLARRGTRFLTGDTCMCCFDCELMPLRLQH 179  
 IENLYS +N+LL HL+KINDHLA RGTRFLTGDTCMCCFDCELMPLRLQH  
 Sbjct: 125 IENLYSKLKLMLVKKDENKNNALLVHLQKINDHLAARGTRFLTGDTCMCCFDCELMPLRLQH 184

Query: 180 IRVAAKYFVEFEIPSNLTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQQQRISNNQMM 239  
 IRVA KYFV+F+IP +LTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQ QM+  
 Sbjct: 185 IRVAGKYFVDFDIPKHLTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQ-----QML 237

Query: 240 KMKKHEELETPTFTTSIPVDVS 261  
 KMKKHEELETPTFTTSIPVD++  
 Sbjct: 238 KMKKHEELETPTFTTSIPVDLN 259

31200365  
 >gi|31200365|ref|XP\_309130.1| ENSANGP00000020556 [Anopheles gambiae]  
 gi|30178539|gb|EAA04940.2| ENSANGP00000020556 [Anopheles gambiae str. PEST]

Length = 257

Score = 439 bits (1129), Expect = e-122  
 Identities = 218/262 (83%), Positives = 232/262 (88%), Gaps = 8/262 (3%)

Query: 1 MSDEMQENG-TINGEVPEIELIIKASTIDGRRKGACLFCEYFMDLYLLAELKTISLKVT 59  
 MSDE Q+NG + NG VPEIELIIKASTIDGRRKGACLFCEYFMDLYLLAELKTISLKVT  
 Sbjct: 1 MSDEGQDNGASRNGSVPEIELIIKASTIDGRRKGACLFCEYFMDLYLLAELKTISLKVT 60

Query: 60 TVDMQKPPPDFRTNFEATPPPILIDNGLAVLENDKIERHIMKSVPGGHNLFVQDKEVATL 119  
 TV MQKPPPDFRTNFEAT PPILIDNGLA+LEN+KIERHIMKSVPGG+NLVQDKEVATL  
 Sbjct: 61 TVCMQKPPPDFRTNFEATHPPILIDNGLAILENEKIERHIMKSVPGGYNLFVQDKEVATL 120

Query: 120 IENLYSXXXXXXXXXXXXXXXXSNSLLSHLRKINDHLARRGTRFLTGDTCMCCFDCELMPLRQH 179  
 IENLYS +N+LL HL+KINDHLA RGTRFLTGDTCMCCFDCELMPLRQH  
 Sbjct: 121 IENLYSKLKLMLVKKDENKNNALLVHLQKINDHLAARGTRFLTGDTCMCCFDCELMPLRQH 180

Query: 180 IRVAAKYFVEFEIPSNLTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQQQRISNNQMM 239  
 IRVA KYFV+F+IP +LTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQ QM+  
 Sbjct: 181 IRVAGKYFVDFDIPKHLTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQ-----QML 233

Query: 240 KMKKHEELETPTFTTSIPVDVS 261  
 KMKKHEELETPTFTTSIPVD++

☐  
 Sbjct: 234 KMKKHEELETPTFTTSIPVDLN 255  
 18859677  
 >gi|18859677|ref|NP\_572928.1|  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=18859677\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=18859677[pgi])  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=18859677\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=18859677[pgi]) CG10997-PA

☐  
 [Drosophila melanogaster]  
 gi|7292935|gb|AAF48326.1|  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7292935\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7292935[pgi])  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7292935\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=7292935[pgi]) CG10997-PA

☐  
 [Drosophila melanogaster]  
 gi|16185715|gb|AAL13950.1|  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16185715\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16185715[pgi])  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16185715\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=16185715[pgi]) LD46306p  
 [Drosophila melanogaster]  
 Length = 260

Score = 426 bits (1094), Expect = e-118.  
 Identities = 211/261 (80%), Positives = 228/261 (87%), Gaps = 8/261 (3%)

Query: 2 SDEMQE-NGTINGEVPEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTT 60  
 S + QE NG+ +VPEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTT  
 Sbjct: 6 SQSQETNGSSKFDVPEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTT 65

Query: 61 VDMQKPPPDFRTNFEATPPPILIDNGLAVLENDKIERHIMKSVPGGHNLFVQDKEVATLI 120  
 VDMQKPPPDFRTNFEAT PPILIDNGLA+LEN+KIERHIMK++PGG+NLVQDKEVATLI  
 Sbjct: 66 VDMQKPPPDFRTNFEATHPPILIDNGLAILENEKIERHIMKNIPGGYNLFVQDKEVATLI 125

Query: 121 ENLYSXXXXXXXXXXXXXXXXSNSLLSHLRKINDHLARRGTRFLTGDTCMCCFDCELMPLRQHI 180  
 ENLY +N+LLSHLRKINDHL+ R TRFLTGDTCMCCFDCELMPLRQHI  
 Sbjct: 126 ENLYVKLKLMLVKKDEAKNNALLSHLRKINDHLSARNRTRFLTGDTCMCCFDCELMPLRQHI 185

Query: 181 RVAKYFVEFEIPSNLTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQQQRISNNQMMK 240  
 RVA KYFV+FEIP++LTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQQ +K  
 Sbjct: 186 RVAGKYFVDFEIPHTLTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQQS-----LK 238

Query: 241 MKKHEELETPTFTTSIPVDVS 261  
 MKKHEELETPTFTT IP+D+S  
 Sbjct: 239 MKKHEELETPTFTTYIPIDIS 259

39584459

>gi|39584459|emb|CAE72597.1| Hypothetical protein CBG19786  
[Caenorhabditis briggsae]  
Length = 291

Score = 162 bits (410), Expect = 6e-39

Identities = 104/283 (36%), Positives = 143/283 (50%), Gaps = 39/283 (13%)

Query: 4 EMQENGTINGEVPEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTTVDM 63  
++Q NG + P +EL +KAS ID RR GA LFCQE++M+LY L E+ ++V TV++  
Sbjct: 6 QIQSNGGDSLSKPLLELYVKASGIDARRIGADLFCQEFWMELYALYEIGVARVEVKTVNV 65

Query: 64 QKPPPDFRTNFEATPPPILID--NGLAVLENDKIERHIMK-----SVPGGHNLVQDKEV 116  
F+ NF PPI+I+ L +N +IE I +VP LF +D  
Sbjct: 66 NSEA--FKKNFLGAQPPIMIEEEKELTYTDNREIEGRIFHLAKEFNVP----LFEKDPSA 119

Query: 117 ATLIENTLYSXXXXXXXXXXXXXXXXS-----NSLLSHLRKINDHLARRG 157  
IENTLY N + L I+ L+ R  
Sbjct: 120 EKRIENLYRNFKLFLRAKVEFDKGKKEPSRVEDLPAQIKVHYNRVCEQLSNIDQLLSERK 179

Query: 158 TRFLTGD TMCCFDCELM PRLQHIRVAAKYFVEFEIPSNLTALWRYMYHMYQLDAFTQSCP 217  
TR+L G++M +DCELM PRL HIR+ + F+IP N T LW Y+ Y+ AF +SCP  
Sbjct: 180 TRYLLGNSMTEYDCELM PRLHHIRIIGLSLLGFDIPHNFTLWNYILTAYRTAAFIESC 239

Query: 218 ADQDIINHYKLQQQRISNNQMMKMKKHEELETPTFTTSIPVDV 260  
ADQDII+HYK Q +N + E L++PT T +IP V  
Sbjct: 240 ADQDIIHHYKEQLNLFNTN-----QRETLSPTKTHTIPEKV 275

41688549

>gi|41688549|sp|Q8WQA4|EXC4\_CAEE Chloride intracellular channel  
exc-4 (Excretory canal abnormal  
protein 4)  
gi|34559859|gb|AAQ75554.1| EXC-4 [Caenorhabditis elegans]  
gi|38422776|emb|CAD21669.2| C. elegans EXC-4 protein (corresponding  
sequence Y105E8A.22)  
[Caenorhabditis elegans]  
Length = 290

Score = 159 bits (402), Expect = 6e-38

Identities = 103/283 (36%), Positives = 143/283 (50%), Gaps = 40/283 (14%)

Query: 4 EMQENGTINGEVPEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTTVDM 63  
++Q NG + P +EL +KAS ID RR GA LFCQE++M+LY L E+ ++V TV++  
Sbjct: 6 QIQSNGDPQSK-PLLELYVKASGIDARRIGADLFCQEFWMELYALYEIGVARVEVKTVNV 64

Query: 64 QKPPPDFRTNFEATPPPILID--NGLAVLENDKIERHIMK-----SVPGGHNLVQDKEV 116  
F+ NF PPI+I+ L +N +IE I +VP LF +D  
Sbjct: 65 NSEA--FKKNFLGAQPPIMIEEEKELTYTDNREIEGRIFHLAKEFNVP----LFEKDPSA 118

Query: 117 ATLIENTLYSXXXXXXXXXXXXXXXXS-----NSLLSHLRKINDHLARRG 157  
IENTLY N + L I+ L+ R  
Sbjct: 119 EKRIENLYRNFKLFLRAKVEFDKGKKEPSRVEDLPAQIKVHYNRVCEQLSNIDQLLSERK 178

Query: 158 TRFLTGD TMCCFDCELM PRLQHIRVAAKYFVEFEIPSNLTALWRYMYHMYQLDAFTQSCP 217  
+R+L G++M +DCELM PRL HIR+ + F+IP N T LW Y+ Y+ AF +SCP  
Sbjct: 179 SRYLLGNSMTEYDCELM PRLHHIRIIGLSLLGFDIPHNFTLWAYILTAYRTAAFIESC 238

Query: 218 ADQDIINHYKLQQQRISNNQMMKMKKHEELETPTFTTSIPVDV 260

ADQDII+HYK Q +N + E L++PT T +IP V  
Sbjct: 239 ADQDIIHHYKEQMNLFNT-----QRETLQSPTKTHTIPEKV 274

29841261  
>gi|29841261|gb|AAP06293.1| similar to XM\_082732 LD46306p in  
Drosophila melanogaster  
[Schistosoma japonicum]  
Length = 263

Score = 119 bits (299), Expect = 4e-26  
Identities = 68/221 (30%), Positives = 111/221 (50%), Gaps = 10/221 (4%)

Query: 16 PEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTTVDMQKPPPDFRTNFE 75  
P IE +KA+ D + +GACL Q++FM LY L E I+L+VT + M PP ++  
Sbjct: 7 PLIEFFLKAAPSDRKERGAC LISQQWFMTLYCLVEKGLINLRVTPMTMDVPPANYVKLNA 66

Query: 76 ATPPPI-----LID----NGLAVLENDKIERHIMKSVPGGHNLFVQDKEVATLIENLYS 125  
A PI ++D +GL + + +E ++K N + + +V +N  
Sbjct: 67 ARHLPIAWIESGILDGEDASGLVISSTESLETLIKLKCANLNPNAESDVRAAEKNFED 126

Query: 126 XXXXXXXXXXXXXSNSLLSHLRKINDHLARRGTRFLTGD TMCCFDCELM PRLQHIRVAAK 185  
L S L +N +LA + GD + DC+L P+LQH+RVA +  
Sbjct: 127 LYSSLMQYIKNDTKKPLCSVLN LNAYLASAAKPYAMGDEISYVDCQLAPKLQHV RVAGR 186

Query: 186 YFVEFEIPSNTALWRYMYHMYQLDAFTQSCPADQDIINHY 226  
+ F+IP ++ +W Y+ ++Y+L +F SCP +DI+ HY  
Sbjct: 187 AYKNFDIPHDMKHIWYI QNIYKLKSFISSCPTTRDILMHY 227

27894378  
>gi|27894378|ref|NP\_444507.1|  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27894378\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27894378[pgi])  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27894378\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=27894378[pgi]) chloride  
intracellular channel 6; chloride channel form A [Homo

sapiens]  
gi|25990942|gb|AAN76729.1|  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=25990942\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=25990942[pgi])  
[http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=25990942\[pgi\]](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=25990942[pgi]) chloride  
channel form A [Homo sapiens]  
Length = 686

Score = 115 bits (287), Expect = 1e-24  
Identities = 73/243 (30%), Positives = 117/243 (48%), Gaps = 27/243 (11%)

Query: 13 GEVPEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTTVDMQKPPPDFRT 72  
G+ +I L +KA DG G C F Q FM L+L K + VTTVD+++ P D +  
Sbjct: 448 GQEH DITLFVKAG-YDGESIGNCPFSQRLFMILWL----KGVIFNVTTVDLKRKPADLQN 502

Query: 73 NFEATPPPILIDNGLAVLENDKIERHIMKSV--PGGHNLFVQDKEVATLIENLYSXXXXX 130  
T PP + +G + +KIE + + + P L Q E + +++  
Sbjct: 503 LAPGTNPPFMTFDGEVKTDVNKIEEFLEEK LAPPRYPKLG TQHPESNSAGNDVFAKFSAF 562

Query: 131 XXXXXXXXS----NSLLSHLRKINDHLAR-----RGTRFLTGD TMCCFD 170  
+ +LL LRK++++L G +FL GD + D  
Sbjct: 563 IKNTKKDANEIHEKNLLKALRKLDNYLNSPLPDEIDAYSTEDVTVSGRKFLDGDDELTLAD 622

Query: 171 CELMPRLQHIRVAAKYFVEFEIPSNTALWRYMYHMYQLDAFTQSCPADQDIINHYKLQQ 230

C L+P+L I++ AK + +FE PS +T +WRY+ + Y D FT +CPADQ+I + Y  
Sbjct: 623 CNLLPKLHIIKIVAKKYRDFEFPSEMTGIWRYLNNAYARDEFTNTCPADQEIEHAYSDVA 682

Query: 231 QRI 233  
+R+

☐

Sbjct: 683 KRM 685

8393147  
>[gi|8393147|ref|NP\\_058625.1|](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=8393147[pgi])  
[http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=8393147\[pgi\]](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=8393147[pgi])  
[http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=8393147\[pgi\]](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=8393147[pgi]) chloride

☐

intracellular channel 5 [Homo sapiens]

[gi|7673566|gb|AAF66928.1|](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=7673566[pgi])  
[http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=7673566\[pgi\]](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=7673566[pgi])  
[http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=7673566\[pgi\]](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=7673566[pgi]) CLIC5 [Homo sapiens]

Length = 251

Score = 114 bits (284), Expect = 3e-24  
Identities = 80/256 (31%), Positives = 127/256 (49%), Gaps = 29/256 (11%)

Query: 5 MQENGTINGEV--PEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTTVD 62  
M ++ T NG+ PEIEL +KA IDG G C F Q FM L+L K + VTTVD  
Sbjct: 1 MTDSATANGDDSDPEIELFVKAG-IDGESIGNCPFSQRLFMILWL----KGVVFNVTVD 55

Query: 63 MQKPPPDFRTNFETPPPIIDNGLAVLENDKIERHIMKSV-PGGH-NLFVQDKEVATLI 120  
+++ P D T PP L NG + +KIE + +++ P + L + +E T  
Sbjct: 56 LKRKPADLHNLAPGTHPPFLT FNQDVKTVDNKKIEEFLEETLTPEKYPKLAAKHRESNTAG 115

Query: 121 ENLYSXXXXXXXXXXXXXXXXXSNL----LSHLRKINDHL-----ARRGTR--F 160  
+++S + +L L+K++D+L +G+R F  
Sbjct: 116 IDIFSKFSAYIKNTKQNNAAALERGLTKALKKKLDDYLNTPLEEDANTCGEDKGSRRKF 175

Query: 161 LTGDTMCCFDCELMPLRQHIRVAAKYFVEFEIPSNLTALWRYMYHMYQLDAFTQSCPADQ 220  
L GD + DC L+P+L +++ AK + ++IP+ +T LWRY+ + Y D FT +C AD  
Sbjct: 176 LDGDELTLADCNLLPKLHVVKIVAKKYRNYDIPAEMTGLWRYLKNAYARDEFTNTCAADS 235

Query: 221 DIINHYKLQQQRISNN 236  
+I Y +R+S +

☐

Sbjct: 236 EIELAYADVAKRLSRS 251

2584785  
>[gi|2584785|emb|CAA73228.1|](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=2584785[pgi])  
[http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=2584785\[pgi\]](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=2584785[pgi])  
[http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=2584785\[pgi\]](http://www.ncbi.nlm.nih.gov/locuslink/list.cgi?Q=2584785[pgi]) p64 bovine  
chloride channel-like protein [Homo sapiens]

Length = 243

Score = 114 bits (284), Expect = 3e-24  
Identities = 76/235 (32%), Positives = 118/235 (50%), Gaps = 31/235 (13%)

Query: 16 PEIELIIKASTIDGRRKGACLFQCEYFMDLYLLAELKTISLKVTTVDMQKPPPDFRTNFE 75  
PEIEL +KA + DG G C FCQ FM L+L K + VTTVDM + P + +  
Sbjct: 12 PEIELFVKAGS-DGESIGNCPFCQRLFMILWL----KGVKFNVTTVDMTRKPEELKDLAP 66

Query: 76 ATPPPILIDNGLAVLENDKIERHIMKSV--PGGHNLFVQDKEVATLIENLYSXXXXXXXX 133  
T PP L+ N + KIE + +++ P +L + KE + NL++  
Sbjct: 67 GTNPPFLVYNKELKTDFIKIEEFLEQTLAPPRYPHLSPKYKESFDVGCNLFKFSAYIKN 126

Query: 134 XXXXXSN----SLLSHLRKINDHL-----ARRGTRFLTGDTCMCCFDC 171  
+ SLL ++++D+L +RR FL GD + DC  
Sbjct: 127 TQKEANKNFEKSLLKEFKRLDDYLNTPLLDEIDPDSAGEPPVSRR--LFLDGDQTLADC 184

Query: 172 ELMPLRQHIRVAAKYFVEFEIPSNTALWRYMYHMYQLDAFTQSCPADQDIINHY 226  
L+P+L I+VAAK + +F+IP+ + +WRY+++ Y + FT +CP D++I N Y  
Sbjct: 185 SLLPKLNIIKVAACKYRDFDIPAEGVWRYLHNAYAREEFTHTCPEDKEIENTY 239